A randomised controlled trial to assess the clinical effectiveness and cost-effectiveness of alternative treatments to Inhibit VEGF in Age-related choroidal Neovascularisation (IVAN)

Usha Chakravarthy,[1]* Simon P Harding,[2] Chris A Rogers,[3] Susan Downes,[4] Andrew J Lotery,[5] Helen A Dakin,[6] Lucy Culliford,[3] Lauren J Scott,[3] Rachel L Nash,[3] Jodi Taylor,[3] Alyson Muldrew,[1] Jayashree Sahni,[2] Sarah Wordsworth,[6] James Raftery,[7] Tunde Peto[8] and Barnaby C Reeves[3] for the IVAN Investigators†

[1]Centre for Experimental Medicine, Institute of Clinical Science, Queen's University Belfast, Belfast, UK
[2]Department of Eye and Vision Science, Institute of Ageing and Chronic Disease, University of Liverpool, Liverpool, UK
[3]Clinical Trials and Evaluation Unit, School of Clinical Sciences, University of Bristol, Bristol, UK
[4]Oxford University Hospitals NHS Trust, Oxford, UK
[5]Clinical and Experimental Sciences, Faculty of Medicine, University of Southampton, Southampton, UK
[6]Health Economic Research Centre, Nuffield Department of Population Health, University of Oxford, Oxford, UK
[7]Wessex Institute, University of Southampton, Southampton, UK
[8]National Institute for Health Research (NIHR) Biomedical Research Centre at Moorfields Eye Hospital NHS Foundation Trust and UCL Institute of Ophthalmology, London, UK

*Corresponding author

†IVAN Investigators are listed in *Appendix 1*.

Declared competing interests of authors: Usha Chakravarthy, Simon P Harding and Andrew J Lotery are principal investigators of trials sponsored by Novartis, the manufacturers of ranibizumab. Usha Chakravarthy has attended and been remunerated for attendance at advisory boards for Novartis, Bayer, Neovista, Oraya, Allergan, and Bausch and Lomb, and her employing institution has received payments from Novartis, Bayer, Neovista, Oraya, Alcon and Pfizer. Chris A Rogers has received an honorarium from Novartis for a lecture. The employing institutions of Susan Downes and Andrew J Lotery have received payments from Novartis. Susan Downes and Andrew J Lotery have received honoraria from Novartis for lectures. Andrew J Lotery has attended and been remunerated for attendance at advisory boards for Novartis and Bayer. Barnaby C Reeves has received a fee for teaching from Janssen-Cilag and is a member of the National Institute of Health Research (NIHR) Health Technology Assessment commissioning board and the NIHR Systematic Reviews Programme Advisory Group. James Raftery is a member of the NIHR Editorial Board and the NIHR Journals Library Editorial Group. He was previously Director of the Wessex Institute and Head of the NIHR Evaluation, Trials and Studies Coordinating Centre.

Published October 2015
DOI: 10.3310/hta19780

Plain English summary

The IVAN trial

Health Technology Assessment 2015; Vol. 19: No. 78
DOI: 10.3310/hta19780

NIHR Journals Library www.journalslibrary.nihr.ac.uk

Plain English summary

The study aimed to compare two drugs (bevacizumab and ranibizumab), and two dosing intensities (injections monthly or intermittently), for treating wet age-related macular degeneration (AMD). Twenty-three hospitals took part. Broadly, we sought to include patients with wet AMD in the study eye, who were older than 50 years. Each participant was allocated one of the drugs and one of the dosing intensities, creating four combinations. The main outcome was the number of letters read on an eye chart using the study eye. Other aspects of eyesight, the appearance of the affected part of the eye, possible harms of treatment, patient-reported outcomes, and resources used to treat participants were measured.

The average improvement in eyesight was very similar with either drug. Monthly treatment was slightly better than intermittent treatment. Quality of life and treatment satisfaction did not differ by drug or dosing intensity. When our results were combined with those of other trials, there was no difference in eyesight outcomes between drugs, but giving treatment monthly was slightly better. Hospitalisations and deaths during the trial occurred equally often with either drug but less often with monthly than intermittent treatment. Ranibizumab was 15 times more expensive than bevacizumab.

Our findings show that the two drugs improve eyesight by a very similar amount and that monthly treatment improves eyesight slightly more than intermittent treatment. Safety appeared to be slightly better when treatment was given monthly. Ranibizumab was not cost-effective compared with bevacizumab. More work is being done on the safety aspects of these drugs and treatment schedules.

Health Technology Assessment

HTA/HTA TAR

ISSN 1366-5278 (Print)

ISSN 2046-4924 (Online)

Impact factor: 5.116

Health Technology Assessment is indexed in MEDLINE, CINAHL, EMBASE, The Cochrane Library and the ISI Science Citation Index.

This journal is a member of and subscribes to the principles of the Committee on Publication Ethics (COPE) (www.publicationethics.org/).

Editorial contact: nihredit@southampton.ac.uk

The full HTA archive is freely available to view online at www.journalslibrary.nihr.ac.uk/hta. Print-on-demand copies can be purchased from the report pages of the NIHR Journals Library website: www.journalslibrary.nihr.ac.uk

Criteria for inclusion in the *Health Technology Assessment* journal

Reports are published in *Health Technology Assessment* (HTA) if (1) they have resulted from work for the HTA programme, and (2) they are of a sufficiently high scientific quality as assessed by the reviewers and editors.

Reviews in *Health Technology Assessment* are termed 'systematic' when the account of the search appraisal and synthesis methods (to minimise biases and random errors) would, in theory, permit the replication of the review by others.

HTA programme

The HTA programme, part of the National Institute for Health Research (NIHR), was set up in 1993. It produces high-quality research information on the effectiveness, costs and broader impact of health technologies for those who use, manage and provide care in the NHS. 'Health technologies' are broadly defined as all interventions used to promote health, prevent and treat disease, and improve rehabilitation and long-term care.

The journal is indexed in NHS Evidence via its abstracts included in MEDLINE and its Technology Assessment Reports inform National Institute for Health and Care Excellence (NICE) guidance. HTA research is also an important source of evidence for National Screening Committee (NSC) policy decisions.

For more information about the HTA programme please visit the website: http://www.nets.nihr.ac.uk/programmes/hta

This report

The research reported in this issue of the journal was funded by the HTA programme as project number 07/36/01. The contractual start date was in July 2007. The draft report began editorial review in January 2014 and was accepted for publication in November 2014. The authors have been wholly responsible for all data collection, analysis and interpretation, and for writing up their work. The HTA editors and publisher have tried to ensure the accuracy of the authors' report and would like to thank the reviewers for their constructive comments on the draft document. However, they do not accept liability for damages or losses arising from material published in this report.

Published by the NIHR Journals Library (www.journalslibrary.nihr.ac.uk), produced by Prepress Projects Ltd, Perth, Scotland (www.prepress-projects.co.uk).